Title: Osteogenic Devices
Inventor(s): Oppermann et al.
Serial No. Not Yet Assigned
Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

FIG. 1A-1

```
10        20        30        40        50        60        70
GGAGGTATAGGAGCTCTCTTCGATTTTAGCAAACCAGGAGTCCGAAGATCTAAGGAGAGCTGGGGGTTTGACTCC
          SacI                                   BglII
85        95        105       115       125       135       145
GAGAGCTCGAGCAGTCCCCAAGACCTGGTCTTGACTCACGAGTTAGACTCCACTCAGAGGCTGACTGTCTCCAGG
SacI              PflMI
   XhoI              Tth111I
160       170       180       190       200       210       220
GTCTACACCTCTAAGGGCGACACTGGGCTCAAGCAGACTGCCGTTTTCTATATGGATGAGCCTTCACAGGGCAG
235       245       255       265       275       285       295
CCAGTTGGGATGGGTTGAGGTTTGGCTGTAGACATCAGAAACCCAAGTCAAATGCGCTTCAACCAGTAGAAAATT
310       320       330       340       350       360       370
CACCAGCCCGCAGAGCTAAGGTTGGGTGGACATTAGGGTTGGTTGATCCAGGAGCTCAACAGTGTCCTCTGAGCC
                                                  SacI
385       395       405       415       425       435       445
CCAGCTCCTTCTGCCCCACCCCACCATCTTCAGTGCTGCTTCCTCTCAAGGCCACAGCTGTAGTTGGCCAGGGGG
                                                    PvuII     BalI
                                                                BglI
460       470       480       490       500       510       520
GCTTCATTATTTTTTGCTCCTGGGCAGTAGGAGGAAGAGAATGAATGTCTCTCCATGGGTCTTTCTTAGGAATGT
                                                     NcoI
535       545       555       565       575       585       595
GGGAACTTTTTCCAGAAGTCTCTATGTCTTTTAGTTTGTGTTGGGTCACTTGCCCTTCCTGAACCACTTCCTGAC
610       620       630       640       650       660       670
TCCTGGACAGGATGTGCACTGATGAGCTTAGCTTTGGGGATCTAATAGTGACTTTACAAAGCCTCTTTGAGAAGG
          ApaLI       EspI
685       695       705       715       725       735       745
TGACATTGGAACCAAGGCTTGAGCAGACACAACAAAGATTGCAGGGAGGGGCATTGCAGGTGGAGGAAACGGCAC
                                                     BspMI-
760       770       780       790       800       810       820
ATGCAAGAGCCCTGCGTGGGAGTGAGCTTGGTGTTTGGTCAATCAGTTGTCAGAGCACACCGGGCCCTGTCAG[illegible]
                                                             ApaI
                                                             EcoO
```

FIG. 1A-2

```
          835      845       855       865       875       885       895
GGCACAGCCTGGGCCTGCTCTGAGTATGACAGAGAGCCCCTGGGAAGTTGTAGGTGGAGGAAAGACAGGTCATGA
           910       920       930       940       950       960       970
CTAGGAAAAAAGCAATCCCTCTGTTGTGGGGTGGAAGGAAGGTTGCAGTGTGTGTGAGAGAGAGACAAGACAGAC
        985       995      1005      1015      1025      1035      1045
AGACAGACACTTCTCAATGTTTACAAGTGCTCAGGCCCTGACCCGAATGCTTCCAAATTTACGTAGTTCTGGAAA
                                 EcoO       BsmI+         SnaBI
       1060      1070      1080      1090      1100      1110      1120
ACCCCCTGTATCATTTTCACTACTCAAAGAAACCTCGGGAGTGTTTTCTTCTGAAAGGTCATCAGGTTTTGACTC
       1135      1145      1155      1165      1175      1185      1195
TCTGCTGTCTCATTTCTTCTTGCTGGTGGTGGTGATGGTTGCTTGTCCCAGGCCCTGTCCCGCATCCTCTTGCCC
                                                    EcoO
       1210      1220      1230      1240      1250      1260      1270
CTGCAGAGGGATGAGTGTGTTGGGGCCTCACGAGTTGAGGTTGTTCATAAGCAGATCTCTTTGAGCAGGGCGCCT
PstI                EcoO                               BglII           NarI Ps
       1285      1295      1305      1315      1325      1335      1345
GCAGTGGCCTTGTGTGAGGCTGGAGGGGTTTCGATTCCCTTATGGAATCCAGGCAGATGTAGCATTTAAACAACA
tI                                                                  DraI
       1360      1370      1380      1390      1400      1410      1420
CACGTGTATAAAAGAAACCAGTGTCCGCAGAAGGTTCCAGAAAGTATTATGGGATAAGACTACATGAGAGAGGAA
       1435      1445      1455      1465      1475      1485      1495
TGGGGCATTGGCACCTCCCTTAGTAGGGCCTTTGCTGGGGGTAGAAATGAGTTTTAAGGCAGGTTAGACCCTCGA
                      EcoO                                 BspMI-
       1510      1520      1530      1540      1550      1560      1570
ACTGGCTTTTGAATCGGGAAATTTACCCCCCAGCCGTTCTGTGCTTCATTGCTGTTCACATCACTGCCTAAGATG
       1585      1595      1605      1615      1625      1635      1645
GAGGAACTTTGATGTGTGTGTGTTTCTTTCTCCTCACTGGGCTCTGCTTCTTCACTTCCTTGTCAATGCAGAGAA
       1660      1670      1680      1690      1700      1710      1720
CAGCAGCAGGCACCAGAGGCAGGCCTTGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGG
                   StuI                                                 BspMI
       1735      1745      1755      1765      1775      1785      1795
TAAGGGGCTGGCTGGGTCTGTCTTGGGTGTGGGCCCTCTGGCGTGGGCTCCCACAGGCAGCGGGTGCTGTGCTCA
                                ApaI
                                EcoO
```

FIG. 1A-3

```
      1810      1820      1830      1840      1850      1860      1870
GTCTTGTTTCTCATCTCTGCCAGTTAAGACTCCAGTATCAAGTGGCCTCGCTAGGGAAGGGTACTTGGCTAAGGA
      1885      1895      1905      1915      1925      1935      1945
TACAGGG.......(APPROX. 1000 BASES)...........GGGAGCCAGCATGGTGATGCCATTATGA
      1960      1970      1980      1990      2000      2010      2020
GTTATTAGCCTCTCTGGCAGGTGGGCAAACCGAGGCATGGAGGTTTGTTTAAGGTGAACTGCCAGTGTGTGACCA
      BglI      BspMI-                                                    Dr
      2035      2045      2055      2065      2075      2085      2095   Pfl
CCTAGTGGGGTAGAGCTGATGATTGCCTCACACCGGAGCTCCTTCCTGTGCCGCGTTCTGTCCAGAAGACACAGC
aIII                                  SacI
MI                                                                         N
      2110      2120      2130      2140      2150      2160      2170
CATGGATGTCCATTTTAGGATCAGCCAAGCCCCGTCTTGTCCTTCATTTTTATTTTATGTTTTTTTAGAAATGGG
coI
      2185      2195      2205      2215      2225      2235      2245
GTCTTGCTCTGTCACCCAGGCTGGGTGCAGTGGTGTGATCATAGCTCACCGCAGCTTTGACGCCGTCTTCCCACT
                                                          Tth111I
      2260      2270      2280      2290      2300      2310      2320
CAGTCTACTAAGCTTGGACTATAGGCCAAGACTATAGAGTGGTCCTTCTTTCCATTCTTTTGGACCATGAGAGG
      HindIII                                        BstXI
      2335      2345      2355      2365      2375      2385      2395
CCACCCATGTTTCCTGCCCCTGCTGGGCCCTGCTGCTCAGAAGGCATGGTCTGAGGCTTTCACCTTGGTCGTGAG
                         ApaI
                         EcoO
      2410      2420      2430      2440      2450      2460      2470
CCTTCGTGGTGGTTTCTTTCAGCATGGGGTTGGGATGCTGTGCTCAGGCTTCTGCATGGTTTCCCACACTCTCTT
      2485      2495      2505      2515      2525      2535      2545
CTCCTCCTCAGGACTGGATCATCGCGCCTGAAGGCTACGCGCGCTACTACTGTGAGGGGGAGTGTGCCTTCCCTC
   MstII                                 BssHII
      2560      2570      2580      2590      2600      2610      2620
TGAACTCCTACATGAACGCCACCAACCACGCCATCGTGCAGACGCTGGTGGGTGTCACGCCATCTTGGGGTGTGG
      2635      2645      2655      2665      2675      2685      2695    Bs
TCACCTGGGCCGGGCAGGCTGCGGGGCCACCAGATCCTGCTGCCTCCAAGCTGGGGCCTGAGTAGATGTCAGCCC
tEII  BglI                                         EcoO
```

FIG. 1A-4

```
   2710      2720      2730      2740      2750      2760      2770
ATTGCCATGTCATGACTTTTGGGGGCCCCTTGCGCCGTTAAAAAAAAATCAAAAATTGTACTTTATGACTGGTTT
                      ApaI
                     EcoO

     2785      2795      2805      2815      2825      2835      2845
GGTATAAAGAGGAGTATAATCTTCGACCCTGGAGTTCATTTATTTCTCCTAATTTTTAAAGTAACTAAAAGTTGT
                                                        DraI
     2860      2870      2880      2890      2900      2910      2920
ATGGGCTCCTTTGAGGATGCTTGTAGTATTGTGGGTGCTGGTTACGGTGCCTAAGAGCACTGGGCCCCTGCTTCA
                                                             ApaI
                                                             EcoO
     2935      2945      2955      2965      2975      2985      2995
TTTTCCAGTAGAGGAAACAGGTAAACAGATGAGAAATTTCAGTGAGGGGCACAGTGATCAGAAGCGGGCCAGCAG
     3010      3020      3030      3040      3050      3060      3070
GATAATGGGATGGAGAGATGAGTGGGGACCCATGGCCATTTCAAGTTAAATTTCAGTCGGGTCACCAGGAAGAT
                       EcoO NcoI                             BstEII
     3085      3095      3105      3115      3125      3135      3145
TCCATGTGATAATGAGATTAACGTGCCCAGTCACGGCGACACTCAGTAGGTGTTATTCCTGCTCTGCCAACAGCA
     3160      3170      3180      3190      3200      3210      3220
ACCATAGTTGATAAGAGCTGTTAGGGATTTTGTCCTTTTGCTTAGAATCCAAGGTTCAAGGACCTTGGTTATGTA
                                                         EcoO
     3235      3245      3255      3265      3275      3285      3295
GCTCCCTGTCATGAACATCATCTGAGCCTTTCCTGCCTACTGATCATCCACCCTGCCTTGAATGCTTCTAGTGAC
                                                          BsmI+
     3310      3320      3330      3340      3350      3360      3370
AGAGAGCTCACTACCAGGACTACTCCCTCCTTTCATTTAGTAATCTGCCTCCTTCTTTTCTTGTCCCTGTCCTGT
  SacI
     3385      3395      3405      3415      3425      3435      3445
GTGTTAAGTCCTGGAGAAAAATCTCATCTATCCCTTTCATTTGATTCTGCTCTTTGAGGCAGGGGTTTTTGTTT
     3460      3470      3480      3490      3500      3510      3520
CTTTGTTTGTTTTTTTAAGTGTTGGTTTTCCAAAGCCCTTGCTCCCCTCCTCAATTGAAACTTCAAAGCCCTCAT
     3535      3545      3555      3565      3575      3585      3595
TGGGATTGAAGGTCCTTAGGCTGGAAACAGAAGAGTCCTCCCCAACCTGTTCCCTGGCCTGGATGTGCTGTGCTG
      EcoOMstII
```

FIG. 1A-5

```
3610        3620        3630        3640        3650        3660        3670
TGCCAGTATCCCCTGGAAGGTGCCAGGCATGTCTCCCCGGCTGCCAGGGGACACATCTCTATCCTTCTCCAACCC
   3685        3695        3705        3715        3725        3735        3745
CTGCCTTCATGGCCCATGGAACAGGAGTGCCATCGCCCTGTGTGCACCTACTTCCATCAGTATTTCACCAGAGAT
  BglI       NcoI                            ApaLI                          BglI
      3760        3770        3780        3790        3800        3810        3820
CTGCAGGATCAAAGTGAATTCTCCAGGGATTGTGAAATGATGCGATTGTGGTCATGTTTAAAAGGGGGCAACTGT
I                 EcoRI                                       DraI
PstI

   3835        3845        3855        3865        3875        3885        3895
CTTCTAGAGAGTCCTGATGAAATGCTTCCAGAGGAAATGAGCTGATGGCTGGAATTTGCTTTAAAATCATTCAAG
  XbaI                                                          DraI
   3910        3920        3930        3940        3950        3960        3970
GTGGAGCAGGTGGGGAAGGGTATGGATGTGTAAGAGTTTGAAATTGTCCATCATAAAATGTGTAAAAAGCATGCT
     BspMI-                                                              SphI
   3985        3995        4005        4015        4025        4035        4045
GGCCTATGTCAGCAGTCACAGCCTGGAGGTGGTAACAGAGTGCCAGTCACTGATGCTCAAGCCTGGCACCTACAG
   4060        4070        4080        4090        4100        4110        4120
TTGCTGGAAACCCAGAAGTTTCACGTTGAAAACAACAGGACAGTGGAATCTCTGGCCCTGTCTTGAACACGTGGC
   4135        4145        4155        4165        4175        4185        4195
AGATCTGCTAACACTGATCTTGGTTGGCTGCCGTCAGCTTAGGTTGAGTGGCGGTCTTCCCTTAGTTTGCTTAGT
BglII

   4210        4220        4230        4240        4250        4260        4270
CCCCGCTATTCCCTATTGTCTTACCTCGGTCTATTTTGCTTATCAGTGGACCTCACGAGGCACTCATAGGCATTT
   4285        4295        4305        4315        4325        4335        4345
GAGTCTATGTGTCCCTGTCCCACATCCTCTGTAAGGTGCAGAGAAGTCCATGAGCAAGATGGAGCACTTCTAGTG
   4360        4370        4380        4390        4400        4410        4420
GGTCCAAGTCAGGGACACTATTCAGCAATCTACAGTGCACAGGGCAGTTCCCCAACAGAGAATTACCTGGTCCTG
                                  ApaLI
   4435        4445        4455        4465        4475        4485        4495
AATGTCGGATCTGGCCCCTTCCTTCCCCACTGTATAATGTGAAAACCTCTATGCTTTGTTCCCCTTGTCTGCAAA
   4510        4520        4530        4540        4550        4560        4570
ACAGGGATAATCCCAGAACTGAGTTGTCCATGTAAAGTGCTTAGAACAGGGAGTGCTTGGCTTGGGGAGTGTCAC
                                                                           Bs
```

FIG. 1A-6

```
        4585      4595      4605      4615      4625      4635      4645
CTGCAGTCATTCATTATGCCCAGACAGGATGTTTCTTTATAGAAACGTGGAGGCCAGTTAGAACGACTCACCGCT
pMI+
PstI
        4660      4670      4680      4690      4700      4710      4720
TCTCACCACTGCCCATGTTTTGGTGTGTGTTTCAGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCT
            PflMI
        4735      4745      4755      4765      4775      4785      4795
GTGCGCCCACGCAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACA
        4810      4820      4830      4840
GAAACATGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCTCCGA
```

FIG. 1B

```
CONSENSUS PROBE    20         30         40         50         60         70
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGACTGGATCATCGCCCCCGTCG
      **                   ** *** ********  ************** **
TGTAAGAAGCACGAGCTGTATGTCAGCTTCCGAGACCTGGGCTGGCAGGACTGGATCATCGCGCCTGAAG
OP4        28         38         48         58         68         78         88

         80         90        100        110        120        130        140
ACTTCGACGCCTACTACTGCTCCGGAGCCTGCCAGTTCCCCTCTGCGGATCACTTCAACAGCACCAACCA
 ** **    *********    **   **   *****            **  ***  *********
GCTACGCGCGCTACTACTGTGAGGGGGAGTGTGCCTTCCCTCTGAACTCCTACATGAACGCCACCAACCA
         98        108        118        128        138        148        158

        150        160        170        180        190        200        210
CGCCGTGGTGCAGACCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAAGCCCTGCTGCGTGCCCACC
****    ******** *****  **  *** *****      *** **************   ******
CGCCATCGTGCAGACGCTGGTCCACTTCATCAACCCGGAAACGGTGCCCAAGCCCTGCTGTGCGCCCACG
        168        178        188        198        208        218        228

        220        230        240        250        260        270        280
GAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATTCCACCGTGGTGCTGAAGAACTACCAGGAGA
 ****   ******       ** ***  ** **   **** ***   ******** ***         *
CAGCTCAATGCCATCTCCGTCCTCTACTTCGATGACAGCTCCAACGTCATCCTGAAGAAATACAGAAACA
        238        248        258        268        278        288        298

        290        300        310
TGACCGTGGTGGGCTGCGGCTGCCGCTAACTGCA
**   **   ** *** ******* *** **
TGGTGGTCCGGGCCTGTGGCTGCCACTAGCTCCT
        308        318        328
```

Inventor(s):Oppermann et al.
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Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

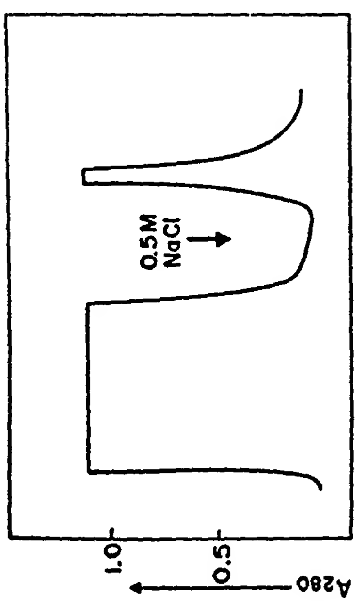


FIG. 2A

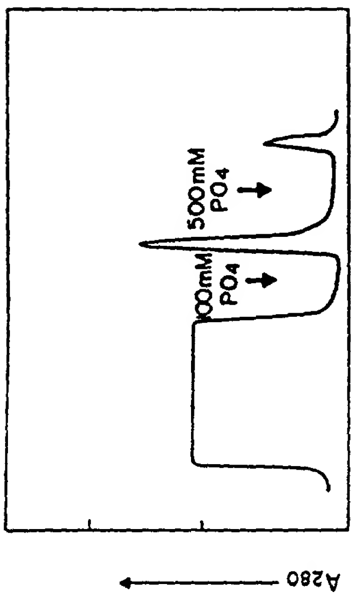


FIG. 2B

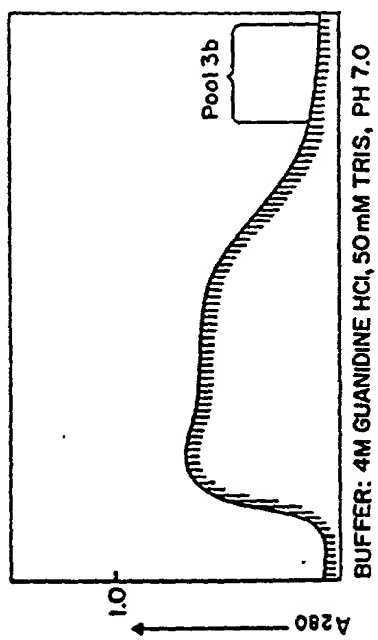


FIG. 2C

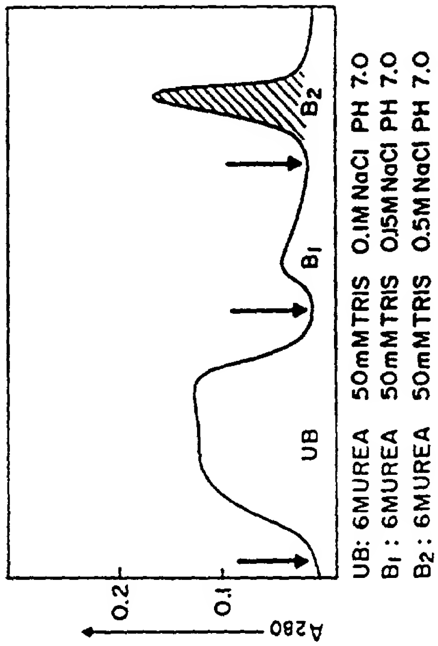


FIG. 2D

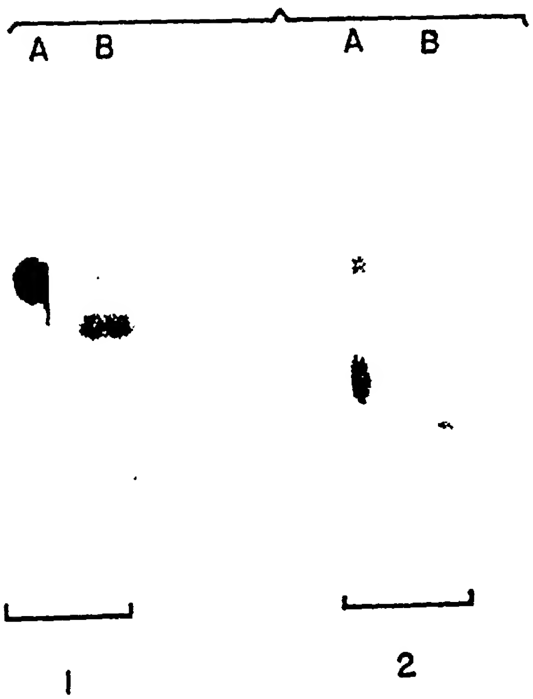
FIG. 3A

FIG. 3B

FIG. 4A

FIG. 4B

FIG. 5



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Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

FIG.6 A FIG. 6 B FIG.6 C FIG. 6 D FIG.6 E

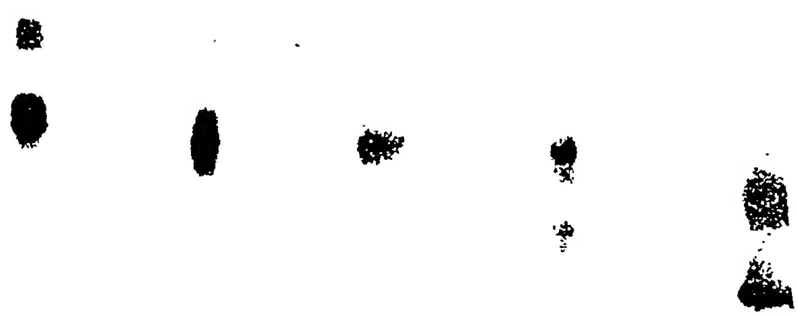
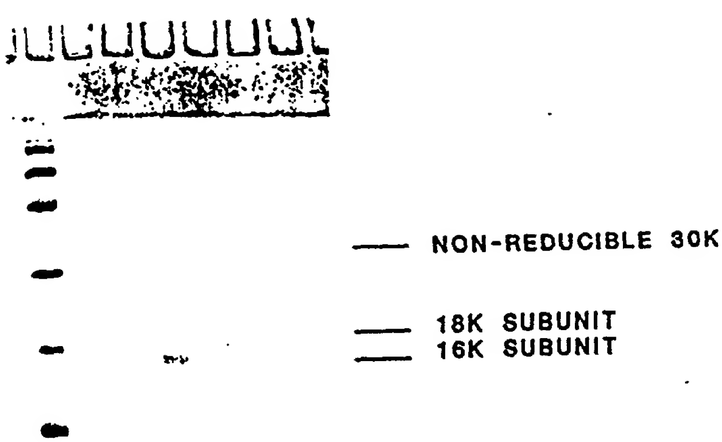


FIG. 15



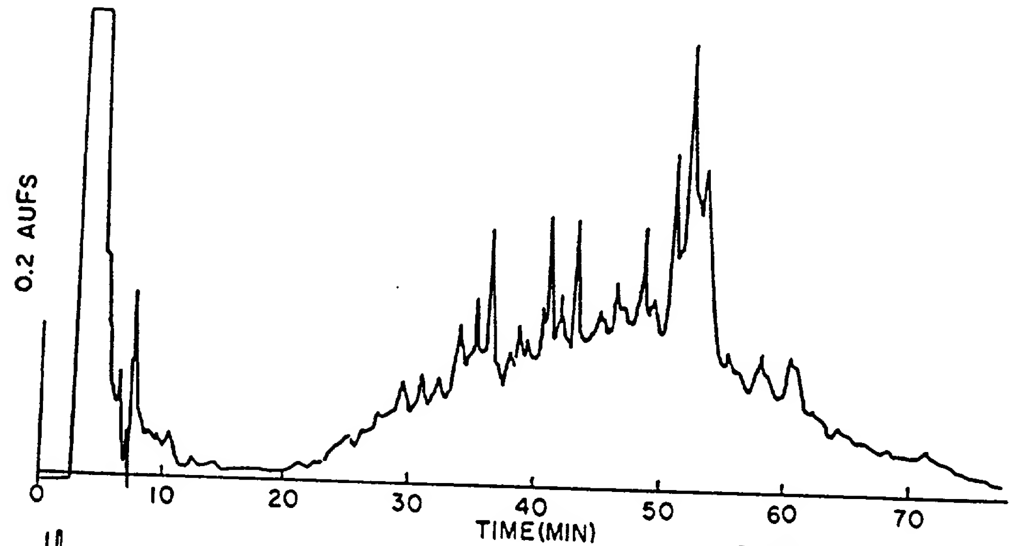


FIG. 7A

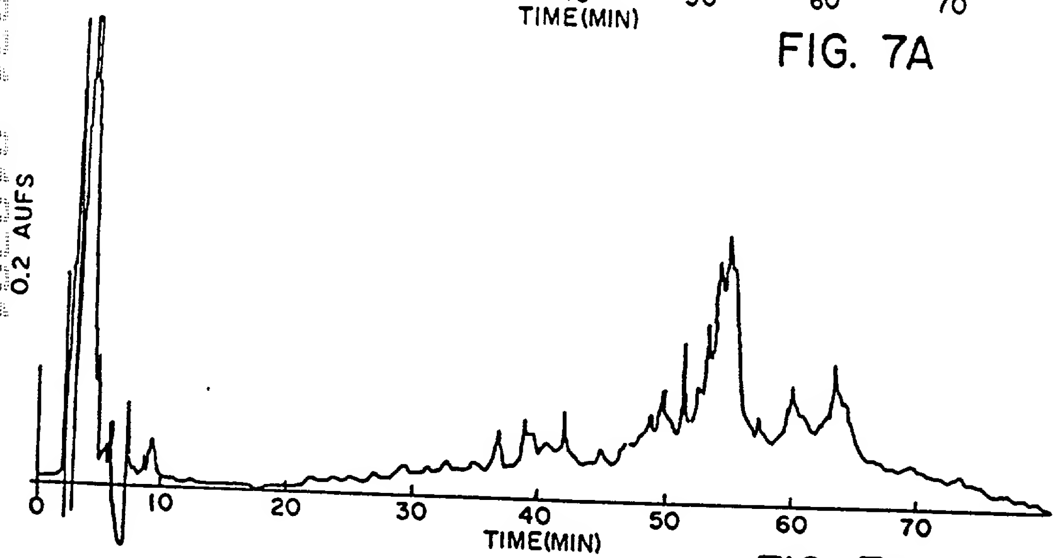


FIG. 7B

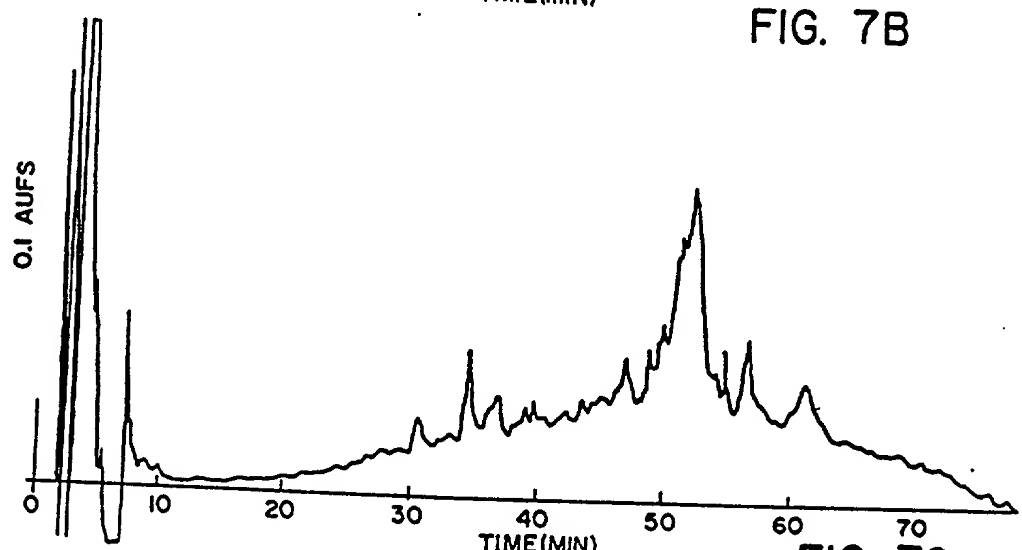


FIG. 7C

Title: Osteogenic Devices
Inventor(s): Oppermann et al.
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Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

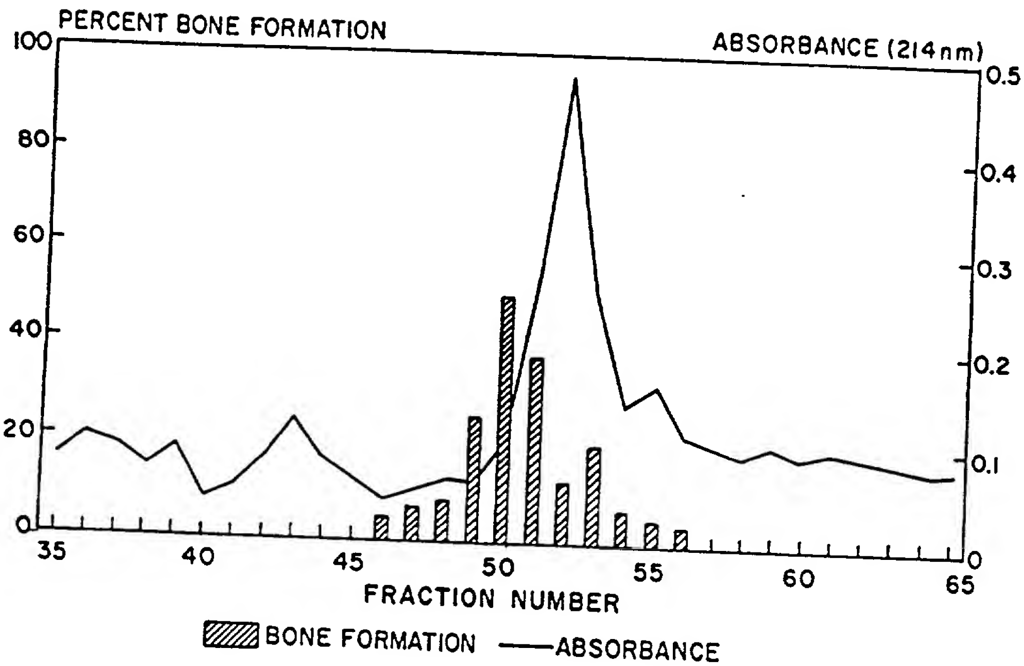

FIG. 8

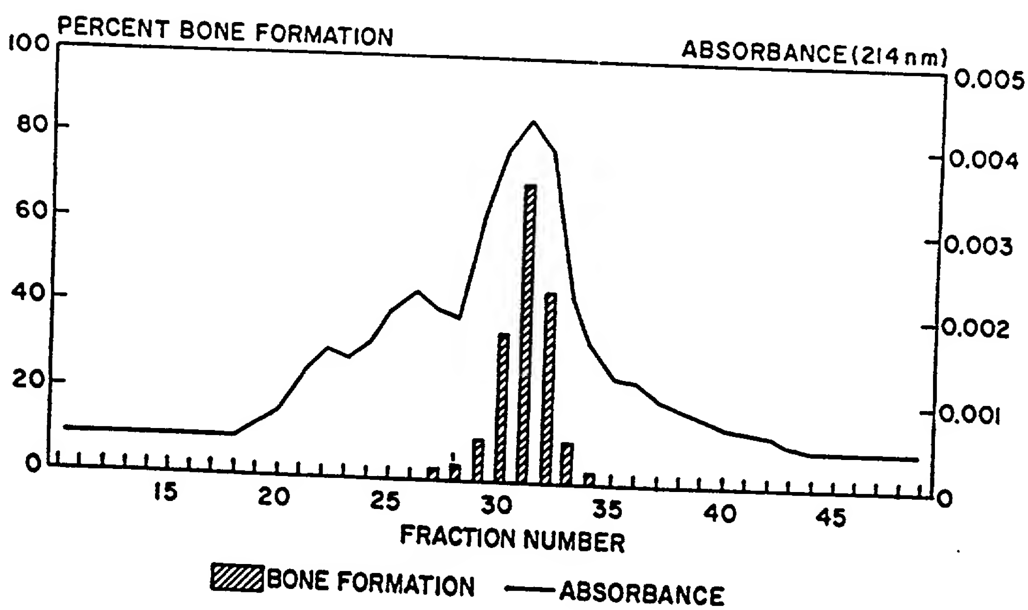

FIG. 9

Title: Osteogenic Devices
Inventor(s): Oppermann et al.
Serial No. Not Yet Assigned
Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

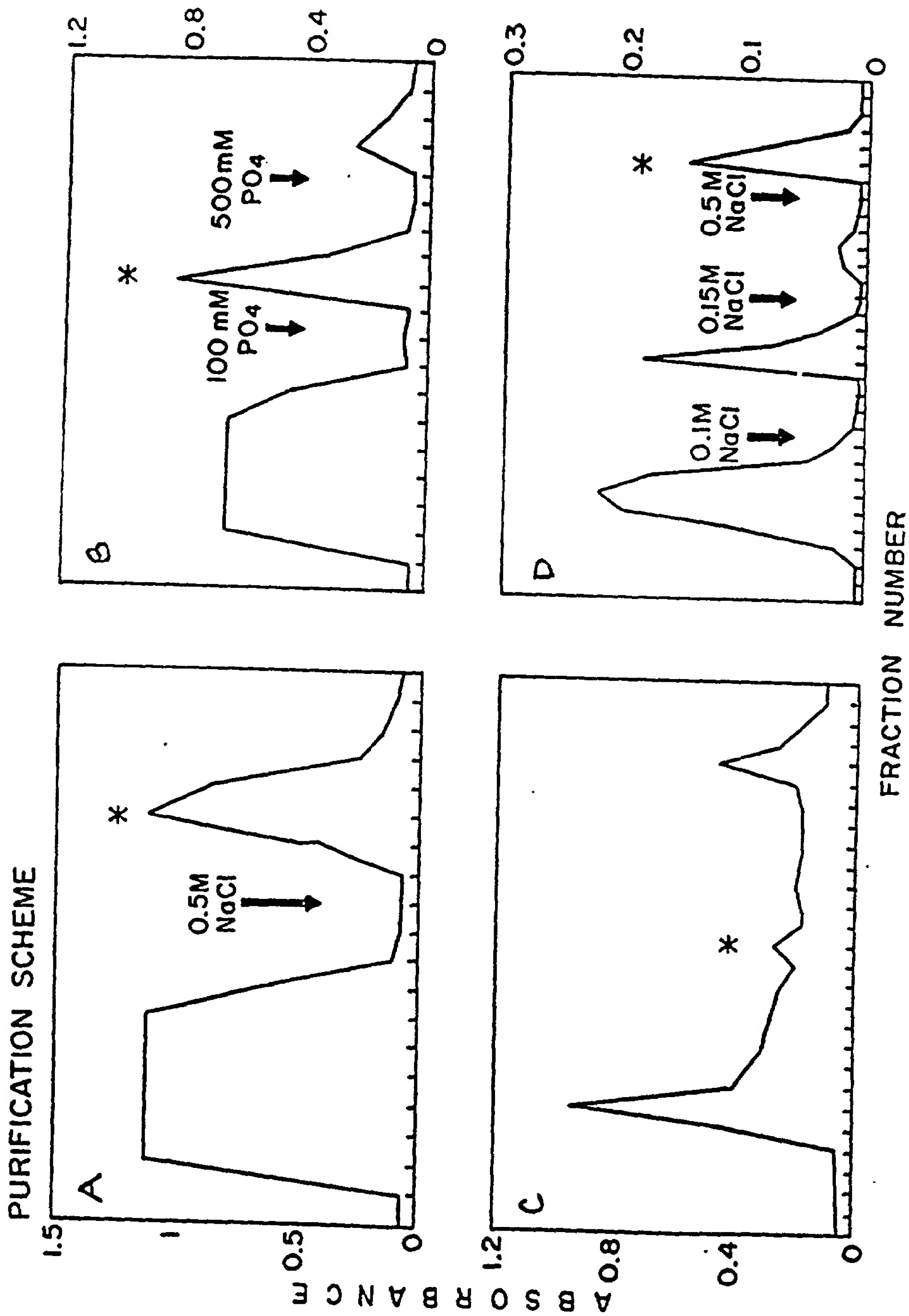

FIG. 10

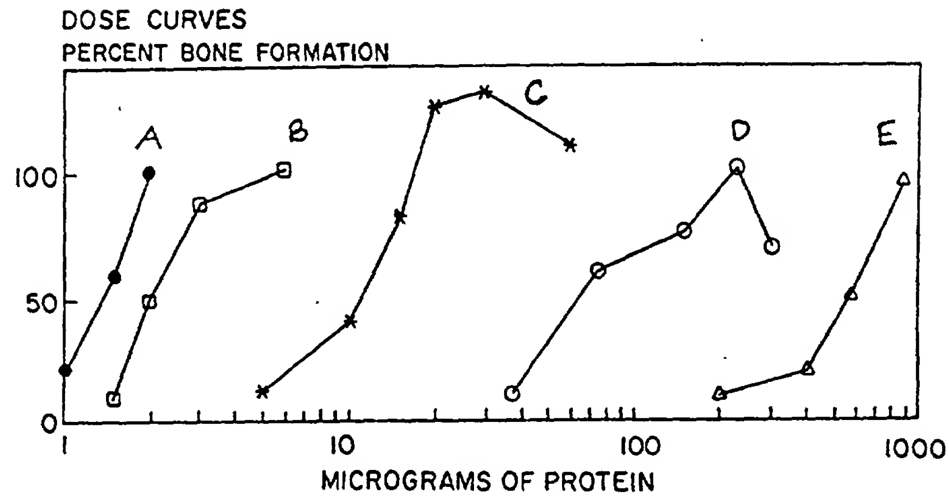
DOSE CURVES
PERCENT BONE FORMATION
A
B
C
D
E
100
50
0
1
10
100
1000
MICROGRAMS OF PROTEIN

FIG. 11

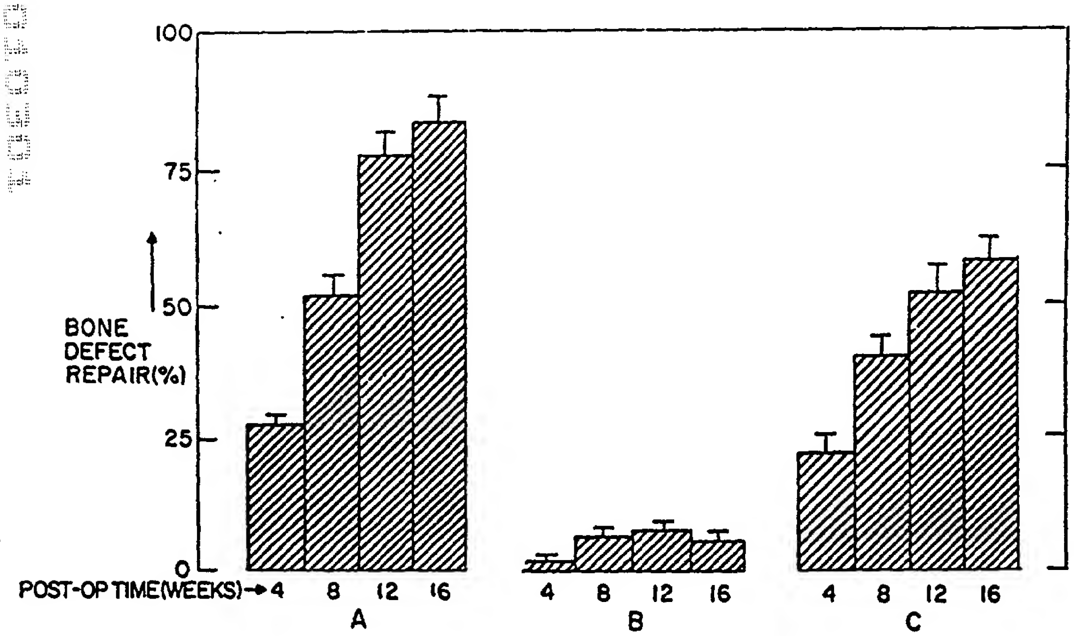
100
75
50
25
0
BONE
DEFECT
REPAIR(%)
POST-OP TIME(WEEKS)→ 4
8
12
16
A
B
C

FIG. 12

genic Devices
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Serial No. Not Yet Assigned
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Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

FIG. 13

```
          10        20        30        40        50
GATCCTAATGGGCTGTACGTGGACTTCCAGCGCGACGTGGGCTGGGACGA
 D  P  N  G  L  Y  V  D  F  Q  R  D  V  G  W  D  D

          60        70        80        90       100
CTGGATCATCGCCCCCGTCGACTTCGACGCCTACTACTGCTCCGGAGCCT
   W  I  I  A  P  V  D  F  D  A  Y  Y  C  S  G  A

         110       120       130       140       150
GCCAGTTCCCCTCTGCGGATCACTTCAACAGCACCAACCACGCCGTGGTG
C  Q  F  P  S  A  D  H  F  N  S  T  N  H  A  V  V

         160       170       180       190       200
CAGACCCTGGTGAACAACATGAACCCCGGCAAGGTACCCAAGCCCTGCTG
 Q  T  L  V  N  N  M  N  P  G  K  V  P  K  P  C  C

         210       220       230       240       250
CGTGCCCACCGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATT
   V  P  T  E  L  S  A  I  S  M  L  Y  L  D  E  N

         260       270       280       290       300
CCACCGTGGTGCTGAAGAACTACCAGGAGATGACCGTGGTGGGCTGCGGC
S  T  V  V  L  K  N  Y  Q  E  M  T  V  V  G  C  G

         310
TGCCGCTAACTGCAG
 C  R  *
```

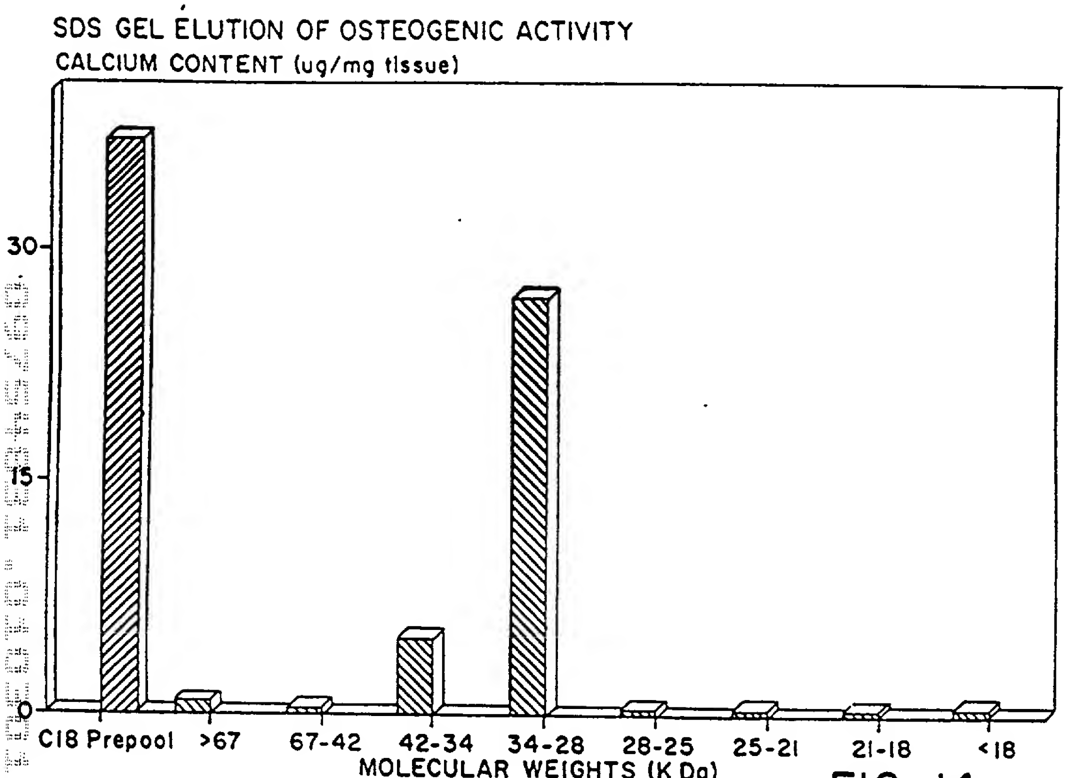
SDS GEL ELUTION OF OSTEOGENIC ACTIVITY
CALCIUM CONTENT (ug/mg tissue)
30
15
0
C18 Prepool
>67
67-42
42-34
34-28
28-25
25-21
21-18
<18
MOLECULAR WEIGHTS (K Da)

FIG. 14

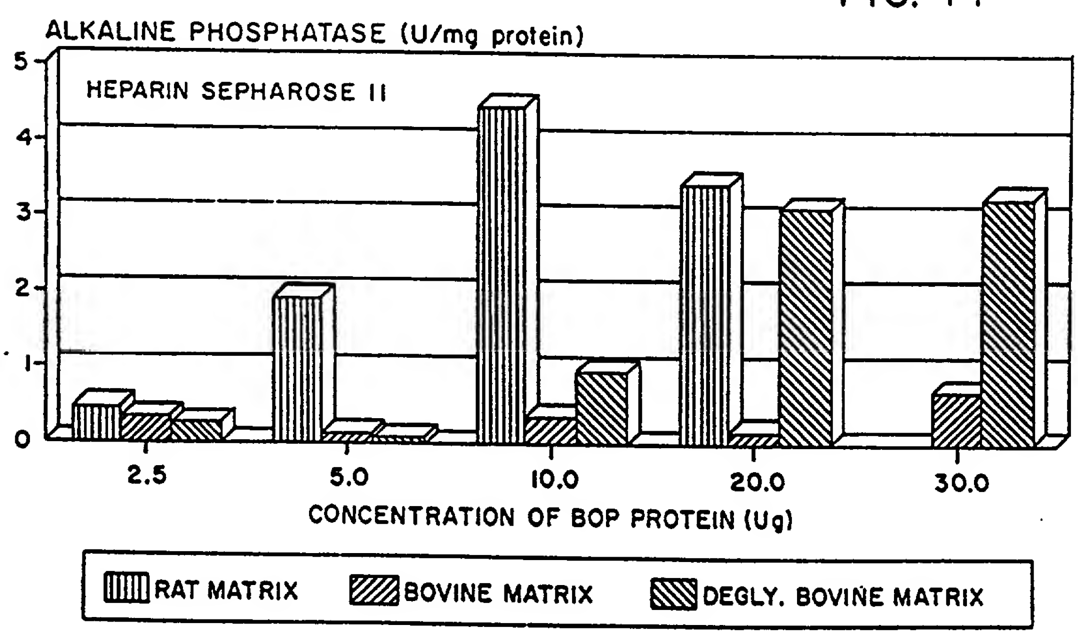
ALKALINE PHOSPHATASE (U/mg protein)
HEPARIN SEPHAROSE II
5
4
3
2
1
0
2.5
5.0
10.0
20.0
30.0
CONCENTRATION OF BOP PROTEIN (Ug)
RAT MATRIX
BOVINE MATRIX
DEGLY. BOVINE MATRIX

FIG. 19

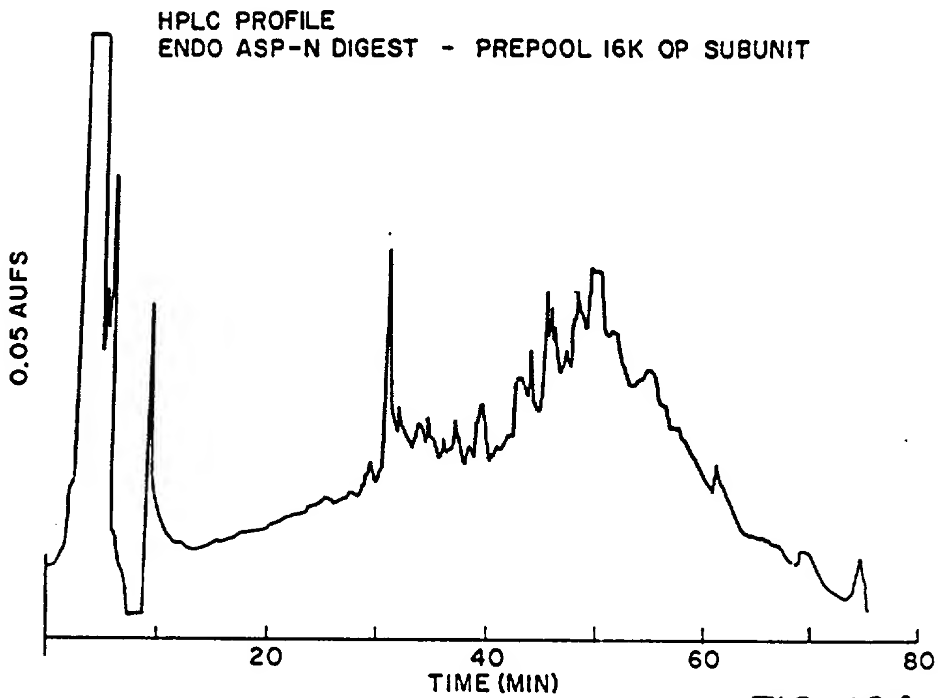

FIG. 16A

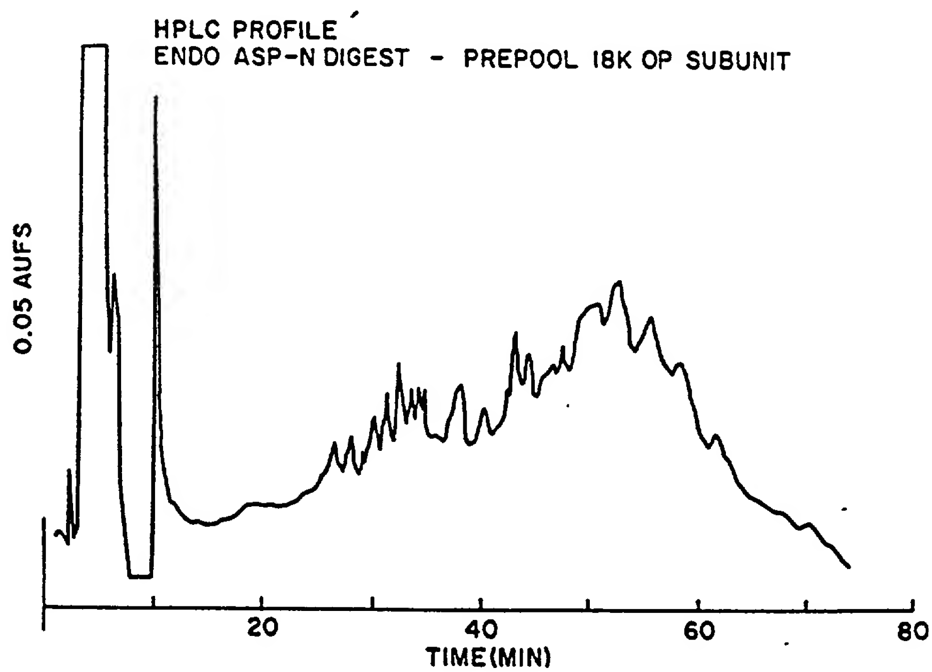

FIG. 16B

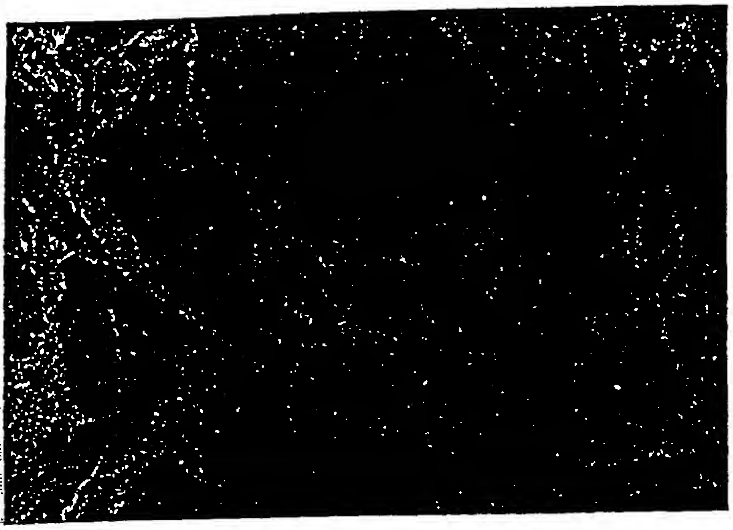

FIG. 17A

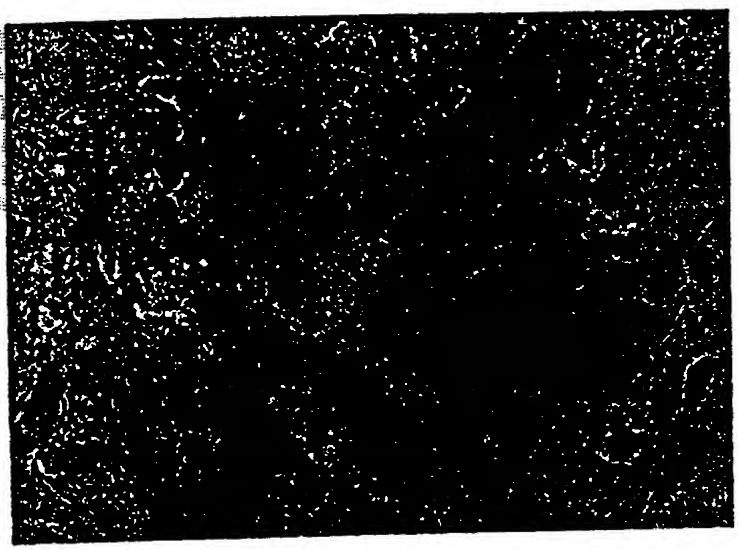

FIG. 17B

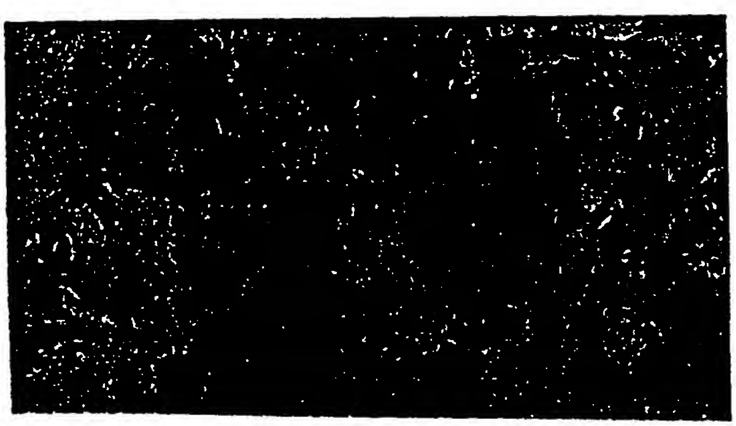

FIG. 17C

COP1	COP3	COP4	COP5	COP7	VG1	DPP	OP1	CBMP2 a)	CBMP2 b)	CBMP3 (bov)	beta-Inhibin a)	beta-Inhibin b)	TGF-beta 1	TGF-beta 2	TGF-beta 3	MIS	alpha Inhib	consensus choices
					C	C	C	C		C	C	C	C			C	C	c
					K	R	K	K	R	A	C	C	C			A	H	k,r
<P	P	P	P	P>	K	R	K	R		R	K	R	V	L	V	L	R	k,r
<N	N	N	N	N>	R	H	H	H		R	K	Q	R			R	V	h,k,r,q
<G	G	G	G	G>	H	S	E	P	S	Y	Q	Q	Q	P	P	E	A	p,s,e,q
L	L	L	L	L	L	L	L	L		L	F	F	L			L	L	l
Y	Y	Y	Y	Y	Y	Y	Y	Y		K	F	F	Y			S	N	y,f
V	V	V	V	V	V	V	V	V		V	V	I	I			V	I	v,i
D	D	D	D	D	E	D	S	D		D	S	D	D			D	S	d,e,s
F	F	F	F	F	F	F	F	F		F	F	F	F			L	F	f
Q	Q	S	S	S	K	S	R	S		A	K	R	R	K	R	R	Q	k,r,s
R	R												K	R	Q	A		
D	D	D	D	D	D	D	D	D		D	D		D			E	E	d
V	V	V	V	V	V	V	L	V		I	I	I	L			R	L	v,l,i
G	G	G	G	G	G	G	G	G		G	G	G	G			S	G	g
W	W	W	W	W	W	W	W	W		W	W	W	W				W	w
D	D	D	D	N	Q	D	Q	N		S	N	N	K				E	q,n,d,e,s
D	D	D	D	D	N	D	D	D		E	D	D	-				R	d,e,n
W	W	W	W	W	W	W	W	W		W	W	W	W				W	w
I	I	I	I	I	V	I	I	I		I	I	I	I	I	V	V	I	i,v
I	V	V	V	V	I	V	I	V		I	I	I	H			L	V	i,v
A	A	A	A	A	A	A	A	A		S	A	A	E			I	Y	a,s
P	P	P	P	P	P	P	P	P		P	P	P	P			P	P	p
V	P	P	P	P	Q	L	E	P		K	S	T	K			E	P	e,q,p*
D	G	G	G	G	G	G	G	G		S	G	G	G			T	S	g,s
F	Y	Y	Y	Y	Y	Y	Y	Y		F	Y	Y	Y			Y	F	y,f
D	Q	Q	Q	H	M	D	V	H		D	H	Y	H	N	Y	Q	I	h,d,n,q,y*
A	A	A	A	A	A	A	A	A		A	A	G	A			A	F	a

FIG. 18-1

Title: Osteogenic Devices
Inventor(s): Oppermann et al.
Serial No. Not Yet Assigned
Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

Y	F	F	F	F	::	N	Y	Y	F	:	Y	N	N	N			:	N	H	:: y,f,n
Y	Y	Y	Y	Y	::	Y	Y	Y	Y	:	Y	Y	Y	F			:	N	Y	:: y,f,n
C	C	C	C	C	::	C	C	C	C	:	C	C	C	C			:	C	C	:: c
S	S	S	H	H	::	Y	H	E	H	:	S	E	E	L	A	S	:	Q	H	:: e,h,*
G	G	G	G	G	::	G	G	G	G	:	G	G	G	G			:	G	G	:: g
A	A	A	E	E	::	E	K	E	E	:	A	E	S	P	A	P	:	V	G	:: e,a*
C	C	C	C	C	::	C	C	C	C	:	C	C	C	C			:	C	C	:: c
Q	Q	Q	P	P	::	P	P	A	P	:	Q	P	P	P			:	G	G	:: p,a,g,q
F	F	F	F	F	::	Y	F	F	F	:	F	S	A	Y			:	W	L	:: f,y
P	P	P	P	P	::	P	P	P	P	:	P	H	Y	I	L	L	:	P	H	:: p
S	S	S	L	L	::	L	L	L	L	:	M	I	L	W	W	R	:	Q	I	:: l,m,i
A	A	A	A	A	::	T	A	N	A	:	P	A	A	S			:	S	P	:: p,a,s,t
D	D	D	D	D	::	E	D	S	D	:	K	G	G				:	D	P	:: d,e,s,g*
H	H	H	H	H	::	I	H	Y	H	:	S	T	V	L			:	R	N	:: h,r,n, s*
F	F	F	F	L	::	L	F	M	L	:	L	S	P	L	S	A	:		L	::m,l,f,p,sa
N	N	N	N	N	::	N	N	N	N	:	K	G	G	D			:	N	S	:: n,k
S	S	S	S	S	::	G	S	A	S	:	P	S	S				:	P	L	:: s,a,p,g
T	T	T	T	T	::	S	T	T	T	:	S	S	A	T			:	R	P	:: t,s,a
N	N	N	N	N	::	N	N	N	N	:	N	L	S	Q	Q	T	:	Y	V	:: n
					::					:		S	S				:	G	P	::
					::					:		F	F				:	N	G	::
H	H	H	H	H	::	H	H	H	H	:	H	H	H	Y	H	H	:	H	A	:: h
					::					:		S	T				:			::
A	A	A	A	A	::	A	A	A	A	:	A	T	A	S			:		P	:: a,t,s
V	V	V	V	V	::	I	V	I	I	:	T	V	V	K	R	T	:	V	P	:: i,v,t
V	V	V	V	V	::	L	V	V	V	:	I	I	V	V			:	V	T	:: v,i,l
Q	Q	Q	Q	Q	::	Q	Q	Q	Q	:	Q	N	N	L			:	L	P	:: q,n
T	T	T	T	T	::	T	T	T	T	:	S	H	Q	A	S	G	:	L	A	:: t, s,a,g
L	L	L	L	L	::	L	L	L	L	:	I	Y	Y	L			:	L	Q	:: l,i
V	V	V	V	V	::	V	V	V	V	:	V	R	R	Y			:	K	P	:: v
N	N	N	N	N	::	H	N	H	N	:	R	M	M	N			:	M	Y	:: h,n r

FIG. 18-2

N	N	N	S	S	::	S	N	F	S		:	A	R	R	Q	T	T:	Q	S	::	n,s *
M	M	M	V	V	::	I	N	I	V		:	V	G	G	H	I	L:	A	L	::	i,v,l,
N	N	N	N	N	::	E	N	N	N		:	G	H	L	N		:	R	L	::	n
					::						:	V	S	N			:	G		::	
					::						:	V					:	A		::	
P	P	P	S	S	::	P	P	P	S		:	P	P	P	P		:	A	P	::	p,s,a
G	G	G			::	E	G	E			:	G	F	G	G	E	E:	L	G	::	g,e
					::						:		A	T	A		:	A		::	
K	K	K	K	K	::	Q	K	T	K	S	:		N	K	S		:	R		::	k,q,t,s
V	V	V	I	I	::	I	V	V	I		:	I	L	V	A		:			::	i,v,l
P	P	P	P	P	::	P	P	P	P		:	P			A	S	S:	P	A	::	p,a,s
K	K	K	K	K	::	L	K	K	K		:	E	K	N			:		Q	::	k
P	P	P	A	A	::	P	A	A	A		:	P	S	S	P		:	P	P	::	a,p,s
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C		:	C	C	::	c
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C		:	C	C	::	c
V	V	V	V	V	::	V	V	A	V		:	V	V	I	V		:	V	A	::	v,a,i
P	P	P	P	P	::	P	P	P	P		:	P	P	P	P	S	P:	P	A	::	p,s,a
T	T	T	T	T	::	T	T	T	T		:	E	T	T	Q		:	T	L	::	t,e,q
E	E	E	E	E	::	K	Q	Q	E		:	K	K	K	A	D	D:	A	P	::	q,e,d,k*
L	L	L	L	L	::	M	L	L	L		:	M	L	L	L		:	Y	G	::	l,m
S	S	S	S	S	::	S	D	N	S		:	S	R	S	E		:	A	T	::	s,n e,d
A	A	A	A	A	::	P	S	A	A		:	S	P	T	P		:	G	M	::	a,s,p,t
I	I	I	I	I	::	I	V	I	I		:	L	M	M	L		:	K	R	::	i,l,m,v
S	S	S	S	S	::	S	A	S	S		:	S	S	S	P	T	T:	L	P	::	s,a,p,t
M	M	M	M	M	::	M	M	V	M		:	I	M	M	I		:	L	L	::	v,m,i,l
L	L	L	L	L	::	L	L	L	L		:	L	L	L	V	L	L:	I	H	::	l,v,i
Y	Y	Y	Y	Y	::	F	Y	Y	Y		:	F	Y	Y	Y		:	S	V	::	y,f
L	L	L	L	L	::	Y	L	F	L		:	F	Y	F	Y		:	L	R	::	f,l,y
D	D	D	D	D	::	D	N	D	D		:	D	D	D	V	I	V:	S	T	::	d,n
E	E	E	E	E	::	N	D	D	E		:	E	D	D	G		:	E	T	::	d,e,
N	N	N	N	N	::	N	Q	S	N	Y	:	N	G	E	R	K	R:	E	S	::	n,q,y*
E	E	E	E	E	::	D	S	S	E	D	:	K	Q	Y	K	T	T:	R	D	::	e,d,s,t

FIG. 18-3

K	K	K	K	K	::	N	T	N	K		:	N	N	N	P			:	I	G	::	n,k
V	V	V	V	V	::	V	V	V	V		:	V	I	I	K			:	S	G	::	v,i
V	V	V	V	V	::	V	V	I	V		:	V	I	V	V	I	V	:	A	Y	::	v,i
L	L	L	L	L	::	L	L	L	L		:	L	K	K	E			:	H	S	::	l
K	K	K	K	K	::	R	K	K	K		:	K	K	R	Q			:	H	F	::	k,r
N	N	N	N	N	::	H	N	K	N		:	V	D	D	L			:	V	K	::	n,d,k*
Y	Y	Y	Y	Y	::	Y	Y	Y	Y		:	Y	I	V				:		Y	::	y
Q	Q	Q	Q	Q	::	E	Q	R	Q		:	P	Q	P	S			:	P	E	::	q,e,p,r
					::						:							:		TVP	::	
E	E	E	E	E	::	N	E	N	D	E	:	N	N	N	N			:	N	N	::	n,d,e
M	M	M	M	M	::	M	M	M	M		:	M	M	M	M			:	M	L	::	m
V	V	V	V	V	::	A	T	V	V		:	T	I	I	I	I	V	:	V	L	::	v,i,t,a
V	V	V	V	V	::	V	V	V	V		:	V	V	V	V			:	A	T	::	v
E	E	E	E	E	::	D	V	R	E		:	E	E	E	R	K	K	:	T	Q	::	e,d,r,k,
G	G	G	G	G	::	E	G	A	G		:	S	E	E	S			:	E	H	::	g,a,s,e
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C			:	C	C	::	c
G	G	G	G	G	::	G	G	G	G		:	H	G	G	K			:	G	A	::	g,h
C	C	C	C	C	::	C	C	C	C		:	C	C	C	C			:	C	C	::	c
R	R	R	R	R	::	R	R	H	R		:	R	S	A	S			:	R	I	::	r,h,s,a,

FIG. 18-4

Title: Osteogenic Devices
Inventor(s):Oppermann et al.
Serial No. Not Yet Assigned
Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

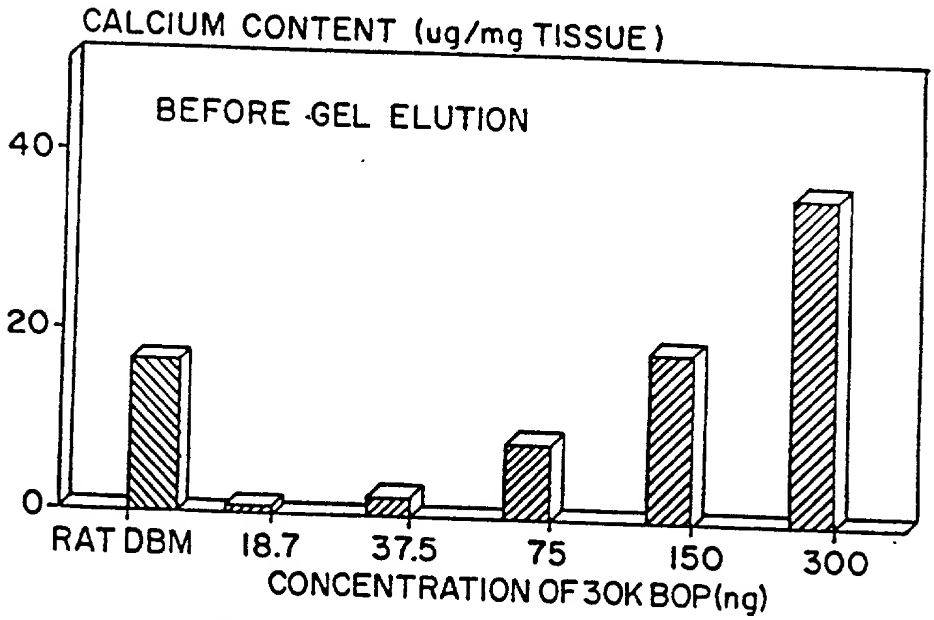

FIG. 20A

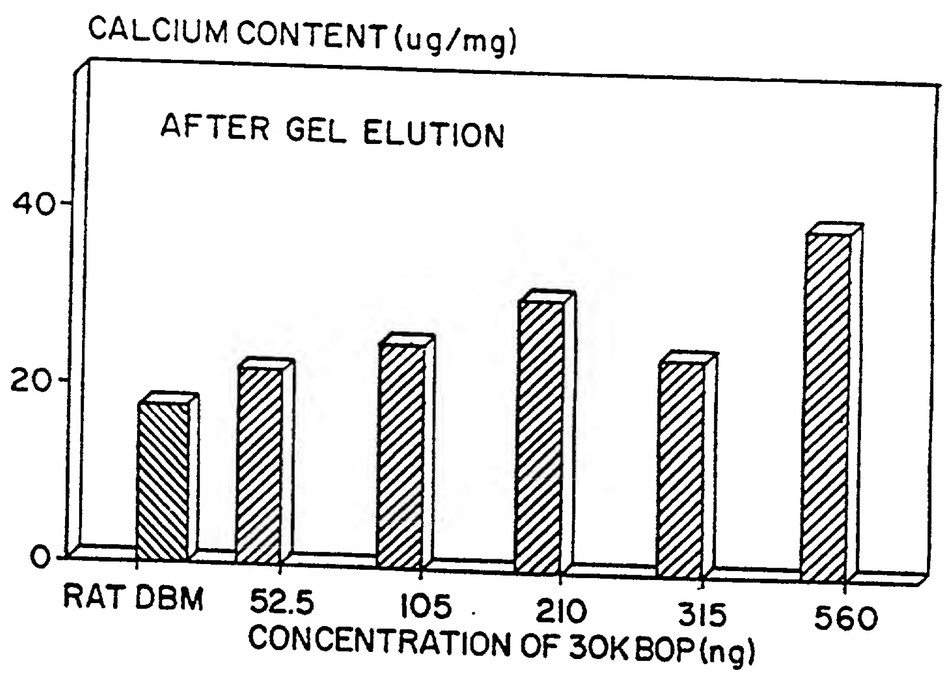

FIG. 20B

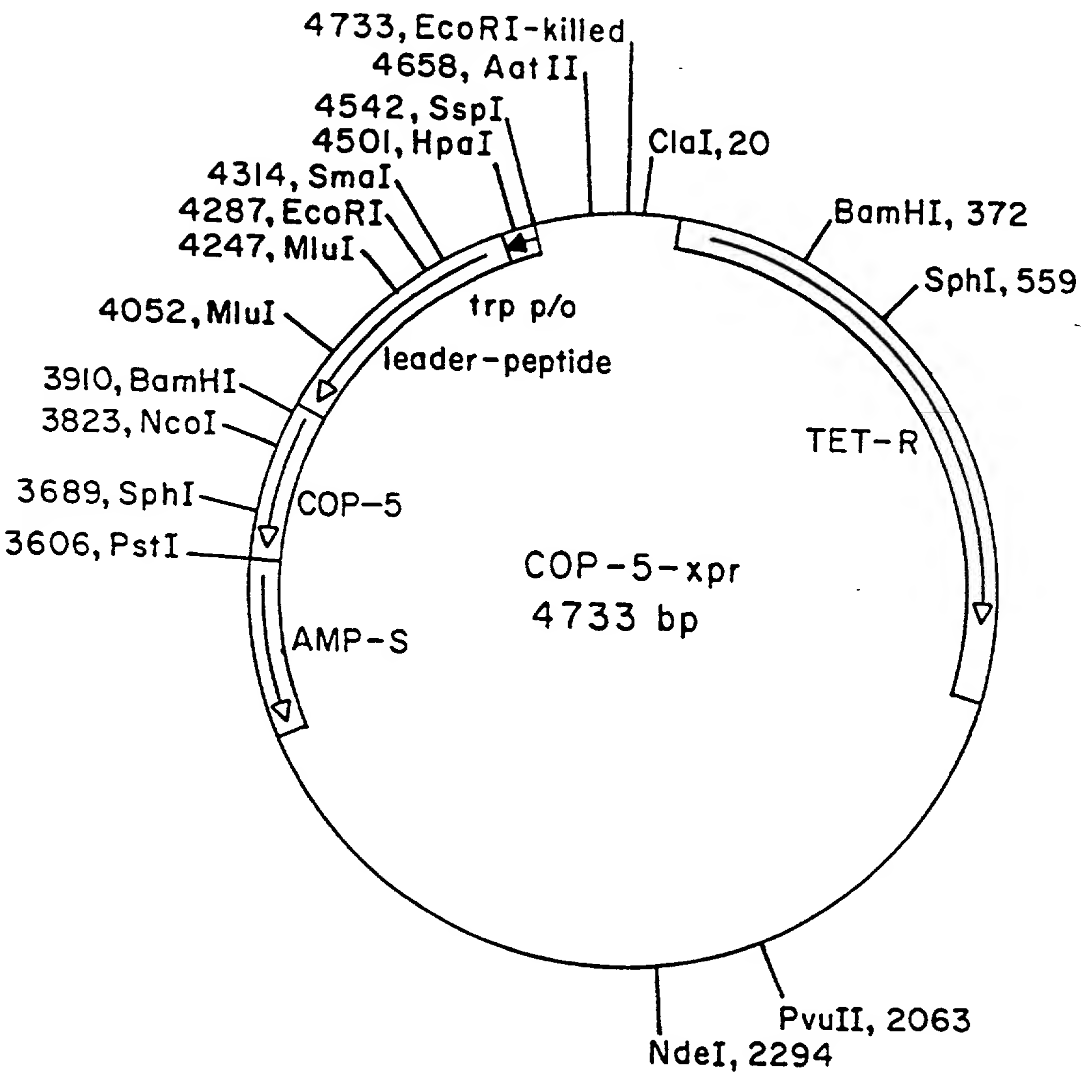
4733, EcoRI-killed
4658, AatII
4542, SspI
4501, HpaI
4314, SmaI
4287, EcoRI
4247, MluI
4052, MluI
3910, BamHI
3823, NcoI
3689, SphI
3606, PstI
ClaI, 20
BamHI, 372
SphI, 559
trp p/o
leader-peptide
COP-5
TET-R
AMP-S
COP-5-xpr
4733 bp
PvuII, 2063
NdeI, 2294

FIG. 21A

COP-5 fusion protein

```
         10        20        30        40        50
ATGAAAGCAATTTTCGTACTGAAAGGTTCACTGGACAGAGATCTGGACTC
 M  K  A  I  F  V  L  K  G  S  L  D  R  D  L  D  S
                                       BglII

         60        70        80        90       100
TCGTCTGGATCTGGACGTTCGTACCGACCACAAAGACCTGTCTGATCACC
  R  L  D  L  D  V  R  T  D  H  K  D  L  S  D  H

        110       120       130       140       150
TGGTTCTGGTCGACCTGGCTCGTAACGACCTGGCTCGTATCGTTACTCCC
L  V  L  V  D  L  A  R  N  D  L  A  R  I  V  T  P
        SalI                                    Sma

        160       170       180       190       200
GGGTCTCGTTACGTTGCGGATCTGGAATTCATGGCTGACAACAAATTCAA
 G  S  R  Y  V  A  D  L  E  F  M  A  D  N  K  F  N
I                         EcoRI

        210       220       230       240       250
CAAGGAACAGCAGAACGCGTTCTACGAGATCTTGCACCTGCCGAACCTGA
  K  E  Q  Q  N  A  F  Y  E  I  L  H  L  P  N  L
                 MluI        BglII     BspMI+

        260       270       280       290       300
ACGAAGAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCT
N  E  E  Q  R  N  G  F  I  Q  S  L  K  D  E  P  S
                             HindIII

        310       320       330       340       350
CAGTCTGCGAATCTGCTAGCGGATGCCAAGAAACTGAACGATGCGCAGGC
 Q  S  A  N  L  L  A  D  A  K  K  L  N  D  A  Q  A
                 NheI                         FspI

        360       370       380       390       400
ACCGAAATCGGATCAGGGGCAATTCATGGCTGACAACAAATTCAACAAGG
  P  K  S  D  Q  G  Q  F  M  A  D  N  K  F  N  K

        410       420       430       440       450
AACAGCAGAACGCGTTCTACGAGATCTTGCACCTGCCGAACCTGAACGAA
E  Q  Q  N  A  F  Y  E  I  L  H  L  P  N  L  N  E
              MluI        BglII     BspMI+

        460       470       480       490       500
GAGCAGCGTAACGGCTTCATCCAAAGCTTGAAGGATGAGCCCTCTCAGTC
 E  Q  R  N  G  F  I  Q  S  L  K  D  E  P  S  Q  S
                        HindIII
```

FIG. 21B-1

```
         510       520       530       540       550
TGCGAATCTGCTAGCGGATGCCAAGAAACTGAACGATGCGCAGGCACCGA
  A  N  L  L  A  D  A  K  K  L  N  D  A  Q  A  P
       NheI                          FspI

        560       570       580       590       600
AGGATCCTAATGGGCTGTACGTCGACTTCAGCGACGTGGGCTGGGACGAC
K  D  P  N  G  L  Y  V  D  F  S  D  V  G  W  D  D
 BamHI               SalI

        610       620       630       640       650
TGGATTGTGGCCCCACCAGGCTACCAGGCCTTCTACTGCCATGGCGAATG
 W  I  V  A  P  P  G  Y  Q  A  F  Y  C  H  G  E  C
                         StuI         NcoI    BsmI+

        660       670       680       690       700
CCCTTTCCCGCTAGCGGATCACTTCAACAGCACCAACCACGCCGTGGTGC
  P  F  P  L  A  D  H  F  N  S  T  N  H  A  V  V
       NheI                          DraIII
                                    PflMI

        710       720       730       740       750
AGACCCTGGTGAACTCTGTCAACTCCAAGATCCCTAAGGCTTGCTGCGTG
Q  T  L  V  N  S  V  N  S  K  I  P  K  A  C  C  V
                               MstII

        760       770       780       790       800
CCCACCGAGCTGTCCGCCATCAGCATGCTGTACCTGGACGAGAATGAGAA
 P  T  E  L  S  A  I  S  M  L  Y  L  D  E  N  E  K
                      SphI

        810       820       830       840       850
GGTGGTGCTGAAGAACTACCAGGAGATGGTAGTAGAGGGCTGCGGCTGCC
  V  V  L  K  N  Y  Q  E  M  V  V  E  G  C  G  C
                    PflMI

        860
GCTAACTGCAG
R  *
   PstI
```

FIG. 21B-2

Title: Osteogenic Devices
Inventor(s):Oppermann et al.
Serial No. Not Yet Assigned
Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

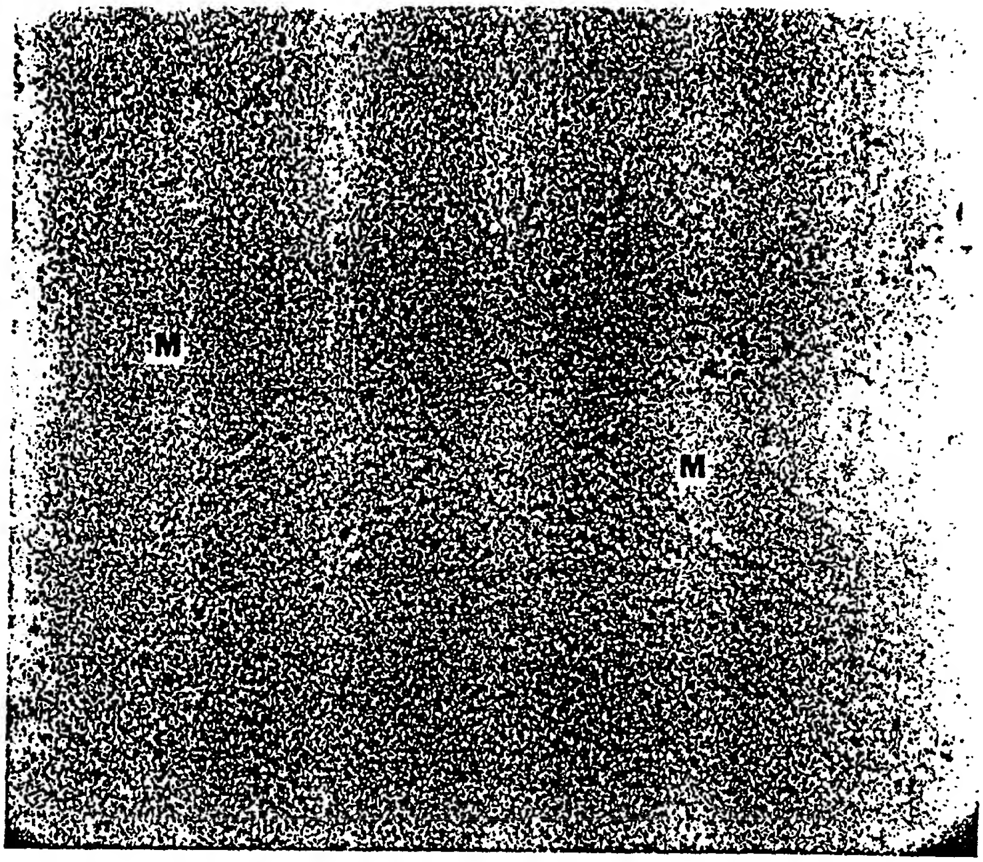

FIG. 22A

Title: Osteogenic Devices
Inventor(s):Oppermann et al.
Serial No. Not Yet Assigned
Atty Docket No. STK-008CN
Atty/Agent: Patrick R. H. Waller
Express Mail Label No. EL280660645US

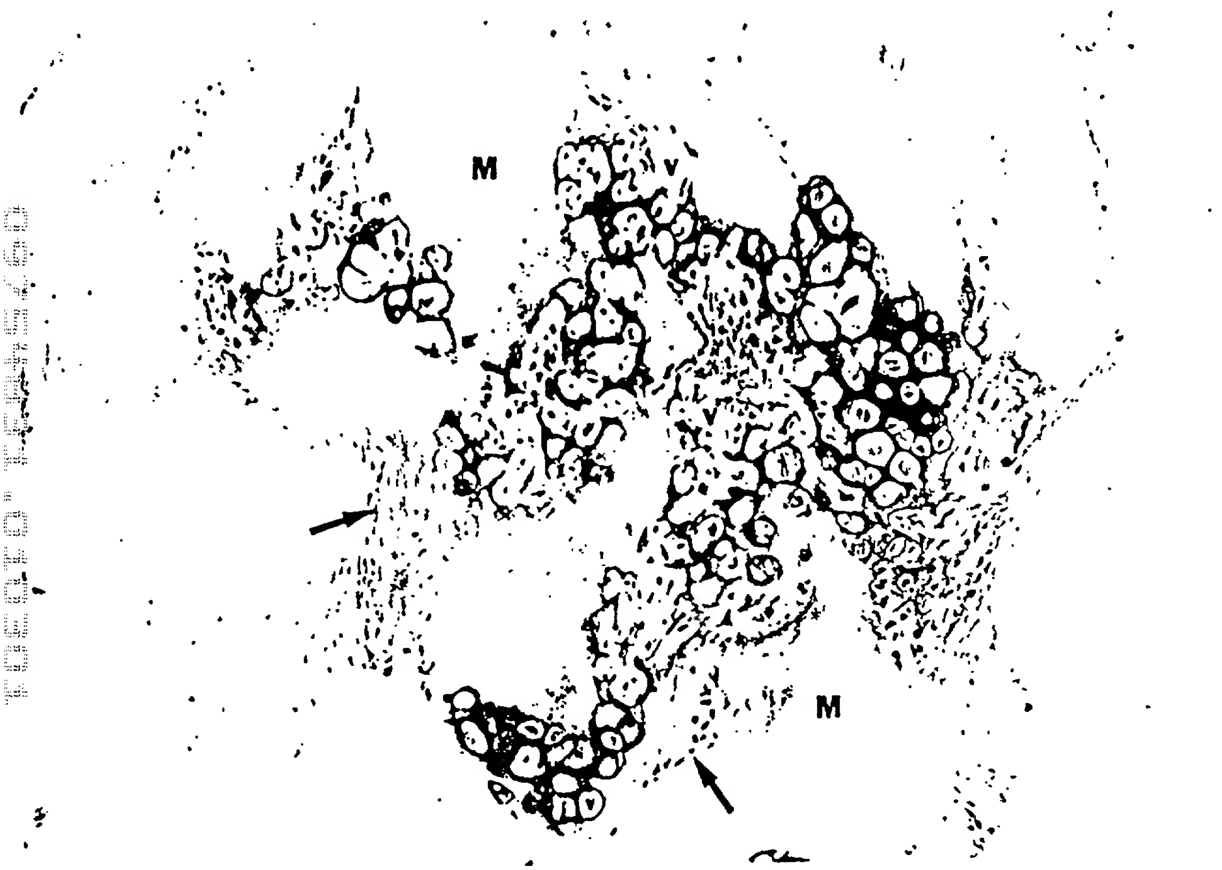

FIG. 22B